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| 09/980,645 | 03/20/2002 | Stefan Anker | 101195-64 | 6782 |

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| HUYNH, PHUONG N | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/980,645 | ANKER ET AL. | |
| | Examiner | Art Unit | |
| | Phuong Huynh | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 6, 17-18, 21, 25-27, 53-55, 58, 69-70, 72-74, 78, and 82-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



HC

Continuation of Disposition of Claims: Claims pending in the application are 1,2,6,11-21,24-27,43,45,47-50,53-55,58,61-63,65-70,72-74 and 76-87.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 11-16,19,20,24,43,45,47-50,61-63,65-68,76,77 and 79-81.

**DETAILED ACTION**

1. Claims 1-2, 6, 11-21, 24-27, 43, 45, 47-50, 53-55, 58, 61-63, 65-70, 72-74, and 76-87 are pending.

2. Claims 11-16, 19-20, 24, 43, 45, 47-50, 61-63, 65-68, 76-77 and 79-81 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

3. Claims 1-2, 6, 17-18, 21, 25-27, 53-55, 58, 69-70, 72-74, 78, and 82-87, drawn to a method of treating or ameliorating chronic heart failure or acute heart failure comprising administering a compound wherein the compound is bile acid that is able to reduce the production, absorption and/or the effect of an endotoxin (LPS) in human blood and a pharmaceutical formulation comprising said bile acid and a diuretic, are being acted upon in this Office Action.

4. In view of the amendment filed 1/13/05, the following objection remains.

5. Claim 53 stands objected to because said claim encompasses non-elected embodiments such as "liver cirrhosis, chronic renal failure, diabetes, rheumatoid arthritis".

6. The following new grounds of rejections are necessitated by the amendment filed 1/13/05.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-2, 6, 17-18, 21, 25-27, 53-55, 58, 69-70, 72-74, 78, and 82-87 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a method of reducing LPS-mediated increase in TNF and IL6 production in whole blood of patients with cachexia due to liver cirrhosis by administering ursodeoxycholic acid in vitro, and (2) a pharmaceutical composition comprising bile acid for reducing LPS-mediated increase in TNF and IL6 production in whole blood of patients with cachexia due to liver cirrhosis, **does not**

reasonably provide enablement for a method of treating or ameliorating chronic heart failure or acute heart failure in any patient comprising administering to the patient any or all "bile acid", any bile acid such as any one of ursodesoxycholic acid, chemdeoxycholic acid, dehydrocholic acid, cholic acid and deoxycholic acid that is able to reduce the production, absorption and/or the "effect" of LPS as set forth in claims 1-2, 6, 17-18, 21, 25-27, 53-55, 58, 69-70, 72-74, 78, and (2) a method of reducing elevated levels of LPS in human blood of patients by administering any amount of "bile acid" effective to reduce the elected levels of LPS in human blood of patient as set forth in claims 82-87. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a method of reducing LPS-mediated increase in TNF and IL6 production in vitro using whole blood of patients with cachexia due to liver cirrhosis by administering ursodeoxycholic acid. The specification further discloses endotoxin LPS and TNF alpha are elevated in patients with chronic heart failure (pages 31-32) which can be detected by ELISA (page 35). The specification suggests that ursodeoxycholic acid (UDCA) *may be* tested in patient with oedema or with cardiac cachexia (page 40). However, no in vivo working example is provided.

The specification does not teach how to make all "bile acids", and pharmaceutical composition comprising all bile acids and "diuretics", much less for treating chronic heart failure or acute heart failure because the term "bile acids" and "diuretics" without the chemical structures or amino acid sequences have no function.

Stryer *et al*, of record, teach that a protein is highly dependent on the overall structure of the protein itself and that the primary amino acid sequence determines the conformational of the protein (See enclosed appropriate pages).

Ngo *et al*, of record, teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (See Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

There is insufficient guidance as to which undisclosed bile acid is able to reduce the production of endotoxin for the claimed method. There is insufficient guidance as to which undisclosed "bile acid" is able to reduce the absorption of endotoxin, much less which bile acid is able to reduce any and all "effect of endotoxin", including any endotoxin mediated immune activation, any response by any cell to endotoxin, any cytokine production and any permeability of the gut wall to bacteria and/or endotoxin such as LPS.

Greve et al teach administering only deoxycholic acid prevents endotoxin related complications such as renal malfunction, other bile acids are less effective. Specifically, deoxycholic acid was the most effective on endotoxin induced tumor necrosis factor production by monocytes, chenodeoxycholic acid was less effective and ursodeoxycholic acid was ineffective. Further, bile acids did not inactivate endotoxin as measured by chromagenic functional Limulus amebocyte assay (see abstract, in particular). Given the indefinite number of undisclosed "bile acid", it is unpredictable which undisclosed "bile acid" has which effect, in turn, is effective for treating or ameliorating chronic or acute heart failure. Even if the pharmaceutical composition is limited to the specific bile acid such as ursodesoxycholic acid, chemdeoxycholic acid, dehydrocholic acid, cholic acid and deoxycholic acid, there is a lack of in vivo working example demonstrating that such bile acid can treat "chronic heart failure" or "acute heart failure", let alone reducing the production, and/or various effects mentioned above.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 1/13/05 have been fully considered but are not found persuasive.

Applicants' position is that Example 12 in the specification describes an in vivo experiment administering a bile acid to patients with cachexia due to liver cirrhosis showing decreased TNF- level in plasma. Example 1 shows that chronic and acute heart failure is caused by increased TNF level in plasma. One of skilled in the art would conclude with these two examples that administering bile acids to a patient suffering from acute and chronic heart failure with increased TNF level will lead to decreasing TNF level in plasma and ameliorating chronic or acute heart failure in the patient.

In response, claim 1 recites a method of treating or ameliorating chronic or acute heart failure by administering bile acid that reduce the production, absorption and/or effect of the endotoxin in human blood. Example 12 merely describes an in vivo experiment administering a bile acid to patients with cachexia due to liver cirrhosis, NOT chronic or acute heart failure as claimed. Further, claim 1 does not recite the a method of treating or ameliorating chronic or acute heart failure by administering bile acid that "reduce the TNF level in plasma". The cited examples are circumstantial evidence at best. There is a lack of in vivo working example demonstrating that any bile acid can treat "chronic or acute heart failure". There is insufficient guidance as to which undisclosed bile acid is able to reduce the production of endotoxin for the claimed method. There is insufficient guidance as to which undisclosed bile acid is able to reduce the absorption of endotoxin, much less which bile acid is able to reduce any and all "effect of endotoxin", including any endotoxin mediated immune activation, any response by any cell to endotoxin, any cytokine production and any permeability of the gut wall to bacteria and/or endotoxin such as LPS. Given the indefinite number of undisclosed "bile acids", it is unpredictable which undisclosed "compound" is effective for treating or ameliorating chronic heart failure. Even if the pharmaceutical composition is limited to the specific bile acid such as any one of ursodesoxycholic acid, chemdeoxycholic acid, dehydrocholic acid, cholic acid and deoxycholic acid, there is a lack of in vivo working example demonstrating that such bile acid can treat chronic heart failure or acute heart failure.

9. Claims 1-2, 6, 17-18, 21, 25-27, 53-55, 58, 69-70, 72-74, 78, and 82-87 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* and *all* "bile acid" that reduce "the production of endotoxin" for a method of treating or ameliorating chronic heart failure or acute heart failure, (2) *any* and *all* "bile acid" that reduce the "effect of endotoxin" for a method of treating or ameliorating chronic heart failure or acute heart failure, (3) any and all "bile acid" that is able to inhibit any or all response by any cell to endothoxin (LPS) for a method of treating or preventing or ameliorating chronic heart failure or acute heart failure, (4) any and all "bile acid" that is able to decrease all cytokine production by all cell in response to LPS for the claimed method, (5) any and all "bile acid" that is able to reduce the permeability of the gut wall to bacteria and/or LPS for the claimed method, (6) any and all "bile acid" that is able reduce the amount of bacteria and/or free endotoxin (LPS) that is able to translocate from the gut into the circulation of the patient for the claimed method, (7) any and all "bile acid" that is able to reduce the permeablility of the gut in patient for the claimed method and (8) any and all "bile acid" and any and all "diuretics" for the claimed pharmaceutical formulation.

The specification discloses only a method of reducing LPS-mediated increase in TNF and IL6 production in vitro using whole blood of patients with cachexia due to liver cirrhosis by administering only ursodeoxycholic acid. The specification further discloses endotoxin LPS and TNF alpha are elevated in patients with chronic heart failure (pages 31-32) which can be detected by ELISA (page 35). The specification suggests that ursodeoxycholic acid (UDCA) may be tested in patient with oedema or with cardiac cachexia (page 40). However, no in vivo working example is provided.

With the exception of the specific ursodesoxycholic acid for a method of reducing LPS-mediated increase in TNF and IL6 production in whole blood of patients with cachexia due to liver cirrhosis by administering ursodeoxycholic acid in vitro, there is inadequate written description about the structure associated with function of all bile acid that has the particular function for treating or ameliorating chronic or acute heart failure mentioned above because the term "bile acid" or "diuretics" without the chemical structure or amino acid sequence has no structure, much less function.

The specification discloses only ursodesoxycholic acid as a method of reducing LPS-mediated increase in TNF and IL6 production in whole blood of patients with cachexia due to liver cirrhosis, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species of compound to describe the genus for the claimed method. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 1/13/05 have been fully considered but are not found persuasive.

Applicants' position is that claim 1 has been amended. The structure of bile acids are known by one skilled in the art.

In response, the specification does not reasonably provide a **written description** of (1) *any* and *all* "bile acid" that reduce "the production of endotoxin" for a method of treating or ameliorating chronic heart failure or acute heart failure, (2) *any* and *all* "bile acid" that reduce the "effect of endotoxin" for a method of treating or ameliorating chronic heart failure or acute heart failure, (3) any and all "bile acid" that is able to inhibit any or all response by any cell to endothoxin (LPS) for a method of treating or preventing or ameliorating chronic heart failure or acute heart failure, (4) any and all "bile acid" that is able to decrease all cytokine production by all cell in response to LPS for the claimed method, (5) any and all "bile acid" that is able to reduce the permeability of the gut wall to bacteria and/or LPS for the claimed method, (6) any and all "bile acid" that is able reduce the amount of bacteria and/or free endotoxin (LPS) that is able to translocate from the gut into the circulation of the patient for the claimed method, (7) any and all "bile acid" that is able to reduce the permeablility of the gut in patient for the claimed method and (8) any and all "bile acid" and any and all "diuretics" for the claimed pharmaceutical formulation.

The specification discloses only a method of reducing LPS-mediated increase in TNF and IL6 production in vitro using whole blood of patients with cachexia due to liver cirrhosis by administering only ursodeoxycholic acid. The specification further discloses endotoxin LPS and TNF alpha are elevated in patients with chronic heart failure (pages 31-32) which can be detected

by ELISA (page 35). The specification suggests that ursodeoxycholic acid (UDCA) *may be* tested in patient with oedema or with cardiac cachexia (page 40). However, no in vivo working example is provided.

10. Claim 78 is rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The "...bile acid *and a diuretic*" in claim 78 represents a departure from the specification and the claims as originally filed. Applicant has not pointed out the support for said phrase in the amendment filed 1/13/05.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 53, 57-58, and 72-73 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0528312A1 (of record, published Oct 4, 1992; PTO 892).

The EP 0528312A1 patent teaches a pharmaceutical composition comprising bile acid such as rusodeoxycholic acid (See page 5, in particular) and a method of treating a patient with liver cirrhosis or chronic hepatopathologies due to hypercholesterol synthesis (page abstract, page 2, first paragraph, in particular). The reference method inherently ameliorating body wasting or cachexia associated with liver cirrhosis since the properties of bile acid in the reference pharmaceutical composition is the same as that of the claimed pharmaceutical composition. Thus, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 1/13/05 have been fully considered but are not found persuasive.

Applicants' position is that the EP document simply discloses oral administration of bile acids and their salts in the treatment of billiary cirrhosis and chronic and cholestatic hepatopathies, but does not teach "reducing elevated LPS levels" in patients by administering bile acid either intravenously, rectally or orally.

In response to arguing limitation "reducing elevated LPS level" which are not claimed, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). See MPEP 2145. Further, the route of administration is within the purview of one skilled in the pharmaceutical to administer orally, rectally or intravenously.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 82-87 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kocsar et al (J Bacteriology 100(1): 220-223, 1969; PTO 892) in view of EP 0528312A1 (of record, published Oct 4, 1992; PTO 892) and

Kocsar et al teach a method of reducing the elevated levels of endotoxin in sera from rat by administering a bile acid such as deoxycholate that reduces the elevated levels of LPS against experimental enterotoxemia (see entire document, abstract, page 222, col. 1 and Table 4, in particular). The reference endotoxin from E. coli that produced fetal shock apparently is the same as the claimed LPS that causes cachexia as evident by page 5 line 7 of the specification.

The invention in claim 82 differs from the teachings of the reference only in that the method of reducing the elevated levels of endotoxin in rat instead of human.

The invention in claim 83 differs from the teachings of the reference only in that the method wherein the bile acid reduces elevated levels of LPS in human blood of patients with cachexia due to liver cirrhosis.

The invention in claim 85 differs from the teachings of the reference only in that the method wherein the bile acid is administered intravenously.

The invention in claim 86 differs from the teachings of the reference only in that the method wherein the bile acid is administered rectally.

The EP 0528312A1 patent teaches a pharmaceutical composition comprising bile acid such as rusodeoxycholic acid (See page 5, in particular) and a method of treating a human patient with liver cirrhosis or chronic hepatopathologies due to hypercholesterol synthesis (page abstract, page 2, first paragraph, in particular).

Bertok et al teach administering sodium deoxycholate resulted in detoxification due to fragmentation of LPS molecule (see page 408, third paragraph, in particular) and that bile acids are significant factors in bacterial LPS detoxification in the liver as well as in the intestines (see page 410, second full paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the rat in the method of reducing elevated levels of LPS as taught by Kocsar et al for the human blood in patients with cachexia due to liver cirrhosis as taught by the EP 0528312A1 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because Bertok et al teach bile acids such as sodium deoxycholate are significant factors in bacterial LPS detoxification in the liver as well as in the intestines (see page 410, second full paragraph, in particular). Deoxycholate is useful in reducing the elevated levels of LPS against experimental enterotoxemia as taught by Kocsar et al (see entire document, abstract, page 222, col. 1 and Table 4, in particular). Claims 85-87 are included in this rejection because the route of administration is within the purview of one of ordinary skilled in the pharmaceutical art to administer any compound orally, intravenously or rectally as taught by Bertok et al.

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (571) 273-8300.

19. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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March 18, 2005